The Effects of Naloxone, Chlorpromazine, and Haloperidol Pretreatment on Levallorphan-Induced Disruption of Rats’ Operant Behaviour

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Abstract. Rats trained on a non-discriminated avoidance procedure (S-S 10 sec, R-S 30 sec) were used to study the effects of naloxone, chlorpromazine and haloperidol pretreatment on levallorphan-induced disruption of bar-pressing behaviour. Levallorphan administration resulted in two highly characteristic effects: cessation of responding for approximately 30 min and a subsequent enhancement of response rates over control values. Chlorpromazine and haloperidol antagonized the cessation of responding, but naloxone failed to do this. Levallorphan-induced rate enhancement was not affected by any of the compounds used.

Key-Words: Naloxone — Neuroleptics — Levallorphan — Psychotomimetic — Operant Conditioning.

Introduction

The narcotic antagonists, cyclazocine, levallorphan and nalorphine produce a wide range of subjective effects in man, some of which resemble those described for LSD (Haertzen, 1970; Jasinski, Martin and Hoeldtke, 1970). In the rat, operant behaviour maintained by punishment or reward is disrupted with some degree of specificity by several well-known psychotomimetics e.g. LSD, mescaline, N,N-diethyltryptamine (DET) and paramethoxy amphetamine (PMA). The administration of these compounds to trained rats is followed by a cessation of responding (pausing) (Appel and Freedman, 1965, 1968; Beaton, Smythies, Benington, Morin and Clark, 1968; Winter, 1969). This interruption does not appear to be a function of muscular weakness, or any other related disability. The pause in responding is followed by a period of hyperactivity resulting in an enhancement of response rates over the corresponding saline levels (Winter, 1969). The present study shows that levallorphan (100 mg/kg, I.P.) produces a similar pattern of behavioural disruption on the shock avoidance behaviour of rats.

The current experiments have investigated the effects of (1) naloxone, (2) chlorpromazine and (3) haloperidol pretreatment, respectively, on
the levallorphan-induced disruption of behaviour in a non-discriminated avoidance situation. Naloxone (N-allylnoroxymorphone), a potent narcotic antagonist with minimal agonist activity, does not produce psychotomimetic effects, miosis, tolerance, physical dependence (Jasinski, Martin and Haertzen, 1967) or appreciable EEG changes in man (Volavka Zaks, Roubicek and Fink, 1970). This compound antagonises the analgesic effects of narcotic antagonists such as cyclazocine, levallorphan and nalorphine in rodents (Blumberg, Dayton and Wolf, 1966), antagonises the depressant effects of cyclazocine (and morphine) on the flexor reflex of the chronic spinal dog (McClane and Martin, 1967) and blocks the pupillary, respiratory depressant, behavioural and subjective effects of cyclazocine in man (Jasinski, Martin and Sapira, 1968). It was therefore of interest to observe if naloxone would similarly influence the behavioural effects of levallorphan in the rat in the non-discriminated avoidance situation.

Chlorpromazine was included for study on the basis of its efficacy as an antipsychotic agent. If the levallorphan-induced disruption of behaviour is in some way related to the human psychotic condition, then it might be expected that chlorpromazine would antagonize this behaviour.

In a previous study (Wray and Cowan, 1971), the present authors suggested that the bizarre-excitatory responses that are seen in rats after levallorphan injection, could be due to the interaction of this drug with dopaminergic mechanisms in the corpus striatum. The butyrophenone neuroleptic, haloperidol, with its reported specific pharmacological action on the dopaminergic system (Van Rossum, 1966; Janssen, 1967; Yeh, McNay and Goldberg, 1969) was considered an appropriate compound to investigate this hypothesis.

Methods

Animals. Naive female hooded rats reared in the animal house of the Department of Psychology, University of Hull, were used in these studies. At the commencement of training each rat was about 120 days old and weighed 200—220 g. Rats were individually housed at a room temperature of 22—24°C, and provided with food and water ad libitum, except during the experimental sessions.

Apparatus. Training and experiments were carried out in Skinner boxes. Each box measured 23.3 × 19 × 27 cm and was individually enclosed in a large sound insulated chamber. The sides of the boxes were made of Perspex; a house light (6 watt bulb) provided constant illumination during training and experimental sessions. The floor was comprised of 18 stainless steel bars, through which brief scrambled